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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,904	11/30/2001	Harold R. Garner	119929-1037	4132

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EXAMINER	
MORAN, MARJORIE A	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 03/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HC

Office Action Summary	Application No.	Applicant(s)	
	09/998,904	GARNER ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may ba availabla under the provisions of 37 CFR 1.136(a). In no avent, however, may a reply be timely filed after SIX (6) MONTHS from tha mailing date of this communication.
- If tha period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will ba considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failura to reply within the set or extended period for reply will, by statuta, causa tha application to becoma ABANDONED (35 U.S.C. § 133). Any reply received by tha Offica later than three months after tha mailing data of this communication, aven if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42, 44-54, 56-213* is/are pending in the application.

4a) Of the above claim(s) *11,13-21,23-36 and 58-213* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,22,37-42,44-54,56,57,203 and 204* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

Election/Restrictions

Claims 11, 13-21, 23-36, and 58-213 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention and/or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in a paper filed 11/3/03..

An action on the merits of elected claims 1-10, 12, 22, and 37-42, 44-54, 56-57, 203 and 204, as they read on the elected species, follows. Claims 43 and 55 have been cancelled.

All rejections and objections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 54 is again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK of WRITTEN DESCRIPTION rejection.

Applicant's arguments filed 10/29/04 have been fully considered but they are not persuasive. In response to the argument that SNIDE is described on pages 6, 26-28 and 30-31 of the specification, it is noted that page 6 merely provides a full term to go with the acronym and does not describe any program steps. Pages 26-27, as previously set forth, discloses that a program termed SNIDE "predicts variants using" at least three steps including (a) input of each codon in a queried DNA sequence; (b) determination of each possible nonsynonymous mutation and (c) assignment of predictiveness. Page 28 of the specification specifically discloses that the novel component of SNIDE "hinges on the statistical methodology" involved. Pages 30-31 of the specification repeatedly disclose use of a "SNIDE algorithm". As previously set forth, the specification is silent with regard to any particular algorithm or "statistical methodology" corresponding to steps of determining *each possible* nonsynonymous mutation and/or assigning predictiveness based on identity of wild-type and resulting codons. Nor does the instant specification disclose anywhere ANY algorithm, or "statistical methodology" for performing the described program steps. Pages 30-31 generally describe SNIDE as an assembly of three PERL scripts which parse input files of DNA data, calculate point mutation probabilities, and rank point mutations. It is noted that these are different from the steps described on pages 26-27. In particular, determination of *each possible nonsynonymous mutation* is not the same as calculating point mutation probabilities, nor is *assignment of predictiveness* based on identity of wild-type and resulting *codons* the same as *ranking of point mutations*. Thus, based on

the instant disclosure, one of skill in the art would not clearly be apprised of just which steps constitute the program called SNIDE.

Page 27 of the specification states that "no technology, other than SNIDE, allows the user to genotype a large sample size for ... SNPs..." On page 28, the specification specifically discloses that the novel component of SNIDE "hinges on the statistical methodology" involved. Thus, SNIDE is disclosed to be a specific computer program. It is noted that independent claim 1 is directed to a method, and parent claim 53 limits the method to one effected by a computer program. The fact that claim 54 limits the computer program to a specific program, with a specific name, further indicates that applicant intends a particular program. A disclosure of general method steps without any description as to an algorithm or specific "statistical methodology" Is not a description of the particular program designated by applicant as SNIDE.

For these reasons and those previously set forth, the rejection is maintained.

Claims 1-10, 12, 22, and 37-42, 44-54, 56-57, 203 and 204 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples;

the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The claims are not enabled because neither the prior art nor specification teaches how to obtain a variation or codon predictiveness matrix such that variations or polymorphisms may be predicted, specifically how to determine a predictiveness value for a single nucleotide polymorphism.

Applicant's arguments filed 10/29/04 have been fully considered but they are not persuasive. The arguments are addressed below.

The prior art provides no guidance on how to obtain or create a variation or codon predictiveness matrix. As previously set forth, the instant specification teaches, on pages 21-22, that statistical analysis may be used to determine the frequency of a *class* of mutations from a mutation database. The specification specifically discloses on page 21, paragraph 59 that for each mutation class, a predictive value was derived that encompasses the "likelihood" that a given point mutation will occur and the impact of that mutation. The specification does not teach how the "likelihood" is calculated nor how to determine the "impact" of the mutation. The specification teaches on page 22 that a "predictiveness value" is the *class's* frequency in a mutation database. The frequency of a class of mutations which appear in a database is not the same as *prediction* of the frequency (likelihood?) of a single (point) mutation. In addition, while the frequency of a mutation in a database may be correlated to its "likelihood" of occurrence, mere frequency does not seem to include or be a determination of "impact". The specification teaches that Table 1B (p. 23) is exemplary of a variation predictiveness matrix, but does not teach any specific method steps, statistical analysis,

or algorithm for arriving at the "predictiveness" values of the Table. Page 25 and Figure 2 disclose calculation of a distribution of codon mutation *classes*, but are not exemplary of a variation predictiveness matrix from which SNP's may be predicted. Applicant argues in the response filed 10/29/04 that original claims 122 and 186now reflected in the specification, "specifically call out" steps of creating a polymorphism predictiveness value and matrix. In response, it is noted that claim 122 recites calculating the mutation rate of a first codon to a second codon in a database of mutant genes, then determining the predictiveness value from the calculated frequency. Claim 186 recites these steps, and a step of generating a matrix correlating the frequency of the first to second codon mutation with the polymorphism predictiveness value. With regard to the first step, it is noted that the database and mutations therein must be known in order to perform the calculation of claims 122 and 186. Thus, the frequency rates calculated are for those particular known sequences ONLY. This is supported by the original specification on pages 21-22, wherein a predictiveness matrix is disclosed based on known sequences from the human genome mutation database. Although a working example of a predictiveness matrix is disclosed, the matrix is actually one for predicting disease, not one which predicts the location of a SNP. As set forth above, the specification does not teach one skilled in the art how to determine a predictiveness value and/or matrix for predicting one or more *locations of SNPs*. It is unknown whether the rate of frequency of mutation is the same for all sequences in all cells or organisms. For example, neither the prior art nor the instant specification teach that the rate of mutation from CAA to CGA is known to be constant in all sequences and environments. Further, it is unclear

how the frequency of mutation of a particular codon to another particular codon (e.g. CGA to CAA) is predictive of the frequency of any other codon to another (e.g. GCU to GAU). Based on the frequency of mutation of CGA to CAA in a kinase encoding gene, how would one skilled in the art determine (or generate a predictiveness value for) the frequency of mutation of GCU to GAU in gene encoding a portion of the GABA receptor? Further, neither the specification nor the claims discloses how a polymorphism predictiveness value is actually "determined" from the calculated frequency value(s). Original claim 186 merely recites that the matrix "correlates" the mutation frequency with a predictiveness value, but the specification does not disclose how one is to perform such a correlation. Is the predictiveness value the same as the frequency; i.e. if the frequency of mutation is 25%, is the predictiveness value 25? Are the frequency values subjected to some statistical manipulation, as is suggested by weighting and normalization steps of page 22?

It is noted that the specification particularly teaches, on page 28, that the "novel component" of the instant invention is the statistical method; however, the specification fails to disclose any particular statistical method or algorithm which results in a matrix for predicting SNPs or sequence "variations". The level of skill in the art is acknowledged to be high. The level of unpredictability in predicting mutations/polymorphisms, specifically SNPs, is also high, as admitted on pages 1-3 of the instant specification. Given the high level of unpredictability in the art for predicting mutations, and the lack of guidance in either the prior art or the specification for how to do so, it would require undue experimentation even for one highly skilled in the art to

obtain a variation predictiveness matrix suitable for predicting variations or polymorphisms using the method steps recited in the claims. For these reasons, the examiner maintains that the claims are not enabled.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-10, 22, 53, and 54-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 54 limits a computer program to be "SNIDE". The specification, on page 6, defines SNIDE as "Single Nucleotide variation Identification". On pages 26-27, the specification describes SNIDE as a "computational method and system" which comprises at least three steps including determination of "each possible nonsynonymous mutation" and "assignment of predictiveness", but does not specifically define a computer program or algorithm to be SNIDE, as set forth above. It is unclear whether applicant intends claim 54 to limit the method of claim 1 to comprise further method steps; e.g. those of pages 26-27 or merely intends the steps of claim 1 to be computer-implemented, or intends the steps of claim 1 to comprise an algorithm, or intends some other limitation, therefore claim 54 is indefinite. Applicant argues on page 12 of the response filed 10/29/04 that the intent is to further limit the method of claim 1 to be computer-implemented. If that is the sole intent of claim 54, then applicant is

advised that claim 54 is duplicative of claim 53, and fails to further limit claim 53, which limits the method of claim 1 to be effected by a computer program. If applicant's intent is to limit the computer program of claim 53 to a specific program, then it is still unclear what particular program, algorithm, etc. is intended, and the examiner maintains that claim 54 is indefinite.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571)

272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
3/3/05